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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,738	STICE, STEVEN	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10 and 12-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,12-14,16-19 and 23-30* is/are rejected.

7)☒ Claim(s) *15 and 20-22* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The response filed October 19, 2007 has been received. The amendment has been entered. However, review of the prosecution history revealed omissions in the office action mailed April 24, 2007. This nonfinal office action corrects those errors. The examiner apologizes for the inconvenience to applicant.

Claim 15 and 20-22 would be allowable if written in independent claims. Presently they are objected to as depending from a rejected independent claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing a cloned nonhuman, nonprimate mammal comprising producing an NT embryo and transferring the NT embryo to a host mammal of the same species for development, does not reasonably provide enablement for method of producing a cloned nonhuman, nonprimate mammal by a means other than transfer to a host mammal of the same species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To produce a cloned mammal, mammalian fetus, or offspring, the NT unit must be transferred to the uterus of a host female mammal of the same species. In vitro methods of fetal development are not enabled by the specification or the art at the time of filing. Thus, an undue amount of experimentation would be required of the skilled artisan to implement the invention as claimed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 9, 10, 14, 16, 17, 19 and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 OR Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning (page 417, col. 2, lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Thus at the time of instant invention, it would have been obvious to the ordinary artisan to modify the method of Cibelli or Prather by synchronizing the cell cycle stage of the donor nuclei to metaphase to match the cell cycle stage of the recipient MII oocyte as taught by Kwon in view of the enhanced success rates of Kwon to produce cows and pigs by nuclear transfer. The ordinary artisan at the time of filing would have known the low success rate of nuclear transfer and would have been motivated to combine the cited art to improve the likelihood of successful nuclear transfer. The prior art provides the requisite teachings, suggestion and motivation to combine.

Claims 1 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and Wakayama et al (1998) Nature, Vol. 394, pp. 369-374 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Wakayama teaches the production of mouse embryos by nuclear transfer, where the nucleus of a cumulus cell was inserted into an enucleated MII arrested oocyte (page 370, col. 1, parag. 1 to page 371, col. 1, parag. 2 col. 3, parag. 1, line 8). Wakayama teaches about 2-3% success rate in producing mice by nuclear transfer.

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning (page 417, col. 2, lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Thus at the time of instant invention, it would have been obvious to the ordinary artisan to modify the method of Cibelli or Prather using cumulus cells as taught by Wakayama and synchronizing the cell cycle stage of the cumulus nuclei to metaphase to match the MII recipient oocyte given the teachings as taught by Kwon. The ordinary artisan at the time of filing would have known the low success rate of nuclear transfer and would

have been motivated to combine the cited art to improve the likelihood of successful nuclear transfer. The enhanced success rate of Kwon provides the motivation required to combine the references.

Claims 1, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and of Campbell et al (1994) Biology of Reproduction, Vol. 50, pp. 1385-1393.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Campbell teaches the production of reconstructed nuclear transfer sheep embryos by the transfer of a donor cell nucleus into the cytoplasm of enucleated oocyte and activating at the time of transfer (page 1389, col. 1, Table 2). Campbell also teaches the production of nuclear transfer sheep embryos by transfer of a donor cell nucleus into the cytoplasm of an enucleated activated sheep oocyte (page 1390, col. 2, parag. 2, lines 1-4). Campbell offers motivation for using recipient oocytes activated at the time of donor nucleus transfer or preactivated oocytes in stating unactivated MII oocytes contain high levels of MPF which may be detrimental to the develop of the reconstructed embryo (page 1390, col. 2, parag. 1, lines 5-14). Lambs developed from reconstructed embryos transferred to surrogate mother sheep, but percentages are not available. Campbell states the decrease in MPF activity in preactivated or activated at the time of transfer prevents abnormal chromosome number in bovine reconstructed oocytes (page 1391, col. 2, lines 1-6).

Thus at the time of instant invention, it would have been obvious to the ordinary artisan to modify the method of Cibelli or Prather and synchronizing the cell cycle stage of donor nuclei to metaphase to match the MII recipient oocyte given the teachings as taught by Kwon, where the MII oocyte was activated at the time of transfer or preactivated in view of Campbell teaching such oocytes give rise to term sheep and in bovines, the percentage of abnormal chromosome number decreases. The ordinary artisan at the time of filing would have known the low success rate of nuclear transfer and would have been motivated to combine the cited art to improve the likelihood of successful nuclear transfer. The prior art provides the requisite teachings, suggestion and motivation to combine.

Claims 1 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci.,

Vol. 93, pp. 13010-13013 Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 in view of Yang et al, (1992) Biol. Reprod. 46, suppl. No. 1, page 117, Abs. 268.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Yang teaches methods of activating matured oocytes in the presence of cycloheximide (lines 4-6). Yang teaches that cycloheximide and electrofusion combined resulted in the activation of 90% of the oocytes (lines 20-27).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning (page 417, col. 2,

lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Thus at the time of the instant invention, it would have been obvious to the ordinary artisan to modify Cibelli or Prather with the teachings of Kwon, where an increase success rate was achieved when metaphase donor nuclei were inserted into MII recipient oocytes, and with the teachings of Yang, where cycloheximide increased the activation rate of oocytes. The ordinary artisan at the time of filing would have known the low success rate of nuclear transfer and would have been motivated to combine the cited art to improve the likelihood of successful nuclear transfer. The prior art provides the requisite teachings, suggestion and motivation to combine.

In the response filed October 19, 2007 applicant indicated they added the limitation of activating the oocyte. However, as indicated in the art rejections Kwon teaches oocyte activation by electric pulse.

Claims 15 and 20-22 are free of the art at the time of filing.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 6:00 AM to 3:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Deborah Crouch

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

December 11, 2007

Pete Ruddy

SPE 1632